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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,136	06/07/2001	Michael G. Walker	PB-0003 USN	5258

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EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/29/2003 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,136	WALKER ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) *9,10 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

Applicant's amendments of claims 2 and 4 in Paper No. 14 filed June 4, 2003, overcome the objection of record of these claims under 35 U.S.C. §132 by removing the new matter objected to in Paper No. 13 mailed March 5, 2003. Claims 9, 10 and 12-15, withdrawn from consideration in Papers 10 and 13 because they are drawn to non-elected subject matter, remain in the application.

New Matter

The amendment filed June 4, 2003, is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to clause (b) of claim 4 stating "an immunogenic fragment of the polypeptide sequence of (a) comprising at least 6 sequential amino acids". Applicant identifies no part of the specification that describes immunogenic hexapeptide fragments of the polypeptide having the amino acid sequence of SEQ ID NO:6. Only the paragraph spanning pages 26-27 of the specification discusses immunogenic peptides, teaching synthesis of decapentapeptides corresponding to regions of SEQ ID NO:6 to be coupled to keyhole limpet hemocyanin to raise antisera. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 4-8 remain rejected for reasons of record under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. Applicant's arguments filed June 4, 2003, have been fully considered together

with the article by Thompson et al., 2002, **Genomics Research**, Vol. 12, pages 1517-1522, but they are not persuasive. It is again noted that the specification and arguments submitted with Papers Nos. 12 and 14 provide no potential utility for subject matters of the genus of polynucleotide products described by clause (c) of claim 2. Applicant argues at pages 6 and 7 of Paper No. 14 that no particular utility need be disclosed for either the disclosed nucleic acid sequence set forth in SEQ ID NO:4 nor its encoded polypeptide having the amino acid sequence set forth in SEQ ID NO:6. Applicant suggests instead that it is a "substantial likelihood" of a "functional association" of expression of a cDNA comprising the sequence of SEQ ID NO:4 with expression of other transcripts "associated with neurotransmitter processing", which provides something useful for the public at the time the specification was filed. The utility of polypeptide and composition of claims 4 and 8 is predicated on the "substantial likelihood" of the proposed "functional association" since inoculation with the products to raise antibodies can be useful only if appearance of the transcript encoding the product is diagnostic of a specific disease state, or prognostic of its treatment, where expression of the transcript by cells produces the polypeptide.

Yet the article by Thompson et al. submitted with Paper No. 14 makes it clear that Applicant's "functional association" is conjecture. Applicant assumes that the polypeptide encoded by SEQ ID NO:4 physically interacts, within neurons or glial cells, with one or more polypeptides encoded by other transcripts that might appear contemporaneously in cells because the transcript comprising the nucleic acid sequence of SEQ ID NO:4, see Table 8 and page 24, lines 12-15, of the specification, occurred in 2% of 522 cDNA libraries surveyed, and in 20% of 45 cDNA libraries having Secretogranin I transcripts, in 24% of 33 cDNA libraries having Secretogranin II transcripts, in 63% of 8 cDNA libraries having vesicular monoamine transporter 1 transcripts, and in 40% of 15 cDNA libraries having L-tyrosine hydroxylase transcripts. Applicant considers these coincidental

detections of transcripts, id., "consistent with the notion that [the cDNA comprising the sequence of SEQ ID NO:4] is associated with neurotransmitter processing", but, unlike the analysis of Thompson et al., Applicant fails to quantitatively confirm the coexpression of the transcript comprising the nucleic acid sequence of SEQ ID NO:4 herein with another transcript that encodes a neurotransmitter-processing polypeptide, or that has been established to be associated with a disease state, using the process of "real-time PCR" in several different cell lines of the same tissue type as shown in Figure 2, page 1520, of Thompson et al. There can be no substantial and credible utility for the products of claim 2 and 4-8 in the absence of a showing in the specification as filed of a substantial, quantitative, association of the claimed nucleic acid sequence encoding the polypeptide of SEQ ID NO:6 with the same constellation, or set, of neurotransmitter processing polypeptide-encoding transcripts in several cultures of neuronal and/or glial cells meeting the standards of Thompson et al.

The investigation of Thompson et al. was also focused on an association of a module, or set, of the transcripts of interest with a specific disease, breast cancer. Applicant generally argues, at pages 7 and 8 of Paper No. 14, that there is a "substantial likelihood" that a set of unspecified interactions of products of unknown function are associated with any one of an assortment of disease states, and that this provides diagnostic utility for a claimed nucleic acid sequence, because transcripts encoding other polypeptide products associated with neurotransmitter processing were detected together with a transcript comprising a claimed nucleic acid sequence encoding the polypeptide of SEQ ID NO:6 in cells of tissue types, neuronal and glial, where the diseases in Applicant's litany arise. Had Applicant performed the same kind of quantitative analysis Thompson et al. completed, Applicant's allegation that the diagnostic or prognostic utility of detecting a transcript comprising SEQ ID NO:4 in a cell is as substantial as the statistical association of Table 8

would still be unsupported by an identification in the specification of a particular disease state with which detection of the claimed transcript comprising the nucleic acid sequence of SEQ ID NO:4 has a specific, credible, association. Thus Applicant's twice-removed "guilt-by-association" analysis – guilt-by-association of a transcript encoding a product having no known function with transcripts in 12 cDNA libraries, two of which encode neurotransmitter-processing products guilty-by-association with certain disorders while the other two do not – cannot define a specific, credible, or substantial utility. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification fails to establish in its disclosure of pages 20-25 that the gene 2823339 transcript, or product, are differentially expressed in CNS neurons, glial cells, or paraganglionic neurons in a normal state versus any specific disease state, or other altered physiological state, and also fails to establish that the 2823339 transcript, or product, are expressed at levels corresponding to levels of the other transcripts indicated in Table 4 in living cells of the nervous system, *in vitro* or *in vivo*. Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific utility that is substantial. The rejection of record is therefore maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4-8 also remain rejected for reasons of record under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a

specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 2 and 4-8 remain rejected for reasons of record under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed June 4, 2003, have been fully considered but they are not persuasive. The amendments of Paper No. 14 have overcome, in part, the rejection of record but clause (c), formerly clause (d), of claim 2 and the amended clause (b) of claim 4 remain subject to the rejection of record. Claims 5-8 are also subject to the rejection of record because they depend from claims 2 and 4. Applicant suggests at pages 10-11 of Paper No. 14 that mere statements, at pages 3 and 8 of the specification, of desired degrees of statistical relationship between disclosed and undisclosed nucleic acid sequences, as well as between disclosed and undisclosed amino acid sequences, would permit one of ordinary skill in the art to identify the sequences that Applicant does not disclose. Yet the statute requires that subject matter must be "described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors" "had possession of the claimed invention" "**at the time the application was filed** (emphasis supplied)." Applicant considers that the ability of the artisan to later identify nucleic acid species, and peptide fragments, that Applicant had failed to identify at the time the application was filed will bestow upon Applicant, rather than the artisan who first describes it, a retroactive possession of compositions of which Applicant provides no evidence showing possession. The specification fails to exemplify or describe the design, preparation, or isolation of nucleic acid sequence products of the clause (d) of claim 2 that diverge in their coding capacity from the elected nucleic acid sequence of SEQ ID NO:4. The specification also fails to exemplify or describe the design or preparation of any immunogenic fragments of clause (b) that are hexapeptides and instead suggests, at pages 26 and 27, that peptide

fragments of SEQ ID NO:6 must be at least 2.5 times larger to be immunogenic. No particular oligopeptides are discussed, and no immunogenic pentadecapeptides are actually described, however. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The Court of Appeals for the Federal Circuit has also held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Unlike the patentee in *Eli Lilly*, Applicant herein declines to state a biological designation of source in the rejected claims yet, just as in the claims invalidated in *Eli Lilly*, seeks to deny the public the practice of inventions Applicant cannot specifically describe where the specification's treatment of subject matters of clause (c) of claim 2 and clause (c) of claim 4 is entirely prospective. The rejection or record is therefore maintained.

Claims 2 and 4-8 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for designing a nucleic acid sequence encoding the polypeptide having the amino acid sequence set forth in SEQ ID NO:6, and for preparing the encoded polypeptide,

does not reasonably provide enablement for designing or preparing a nucleic acid sequence encoding a polypeptide having an amino acid sequence differing from that set forth in SEQ ID NO:6 or for preparing an immunogenic hexapeptide fragment of SEQ ID NO:6 which is a hexapeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed June 4, 2003, have been fully considered but they are not persuasive. The amendments of Paper No. 14 have overcome, in part, the rejection of record but clause (c), formerly clause (d), of claim 2 and the amended clause (b) of claim 4 remain subject to the rejection of record. Claims 5-8 are also subject to the rejection of

record because they depend from claims 2 and 4. With entry of the amendments of Paper No. 14, claim 2 contemplates codon alterations of SEQ ID NO:4 at as many as ten of the amino acid positions therein without any teaching suggesting where, and how, the encoding nucleic acid sequence might be altered to provide a functioning or a useful polypeptide. Applicant argues at pages 15 and 16 of Paper No. 14 that a functional definition of the product encoded by SEQ ID NO:4 is unnecessary because the artisan need only identify a variant, encoding, nucleic acid to arrive at a claimed invention. The scope of the claim is greater, however, because it reaches intentional alteration of the encoding nucleic acid sequence to produce a variant amino acid sequence. Whether an altered coding sequence is intentional or fortuitous, there is no basis in the specification for codon alteration in SEQ ID NO:4 because neither the prior art of record nor Applicant's specification can identify, taken together, a function for the polypeptide SEQ ID NO:6, thus one of ordinary skill in the art seeking to prepare any of the myriad species of encoding polynucleotides, or encoded polypeptides, within the embrace of clause (c) of claim 2, could not determine what to keep, or what and where to discard or alter, in the encoded amino acid sequence to provide a useful product. Immunogenic hexapeptides corresponding to regions of SEQ ID NO:6 described by clause (b) of claim 4 cannot be regarded as enabled when the specification itself teaches that a peptide fragment that is immunogenic must comprise at least a 15-amino acid region of SEQ ID NO:6.

The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see

also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The rejection or record is therefore maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct FAX telephone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
July 21, 2003

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